University of Minnesota
The University Library
Minneapolis 14 Minn.

U.S. POSTAGE
02

UNIVERSITY OF MINNESOTA
NOV
16
1953

CLINICAL PROCEEDINGS

of the

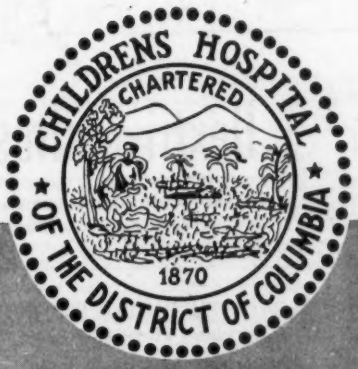
CHILDREN'S HOSPITAL

WASHINGTON, D. C.

SAMPLE COPY

July 1953

VOLUME IX NUMBER 7

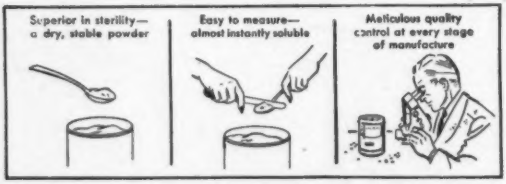


confidence..

For more than forty years, milk and Dextri-Maltose formulas have been used by physicians everywhere with consistently good results. No other carbohydrate used in infant feeding has a comparable record of medical acceptance and clinical effectiveness.

Dextri-Maltose No. 1, for routine infant feeding, is the basic Dextri-Maltose product. Dextri-Maltose No. 2, especially for premature infants, contains 50 mg. ascorbic acid per ounce. Dextri-Maltose No. 3, to aid in counteracting constipation, contains 3% potassium bicarbonate

A formula supplying 20 calories per fluid ounce is easily prepared with 1 part evaporated milk and 2 parts water, plus 1 tablespoon Dextri-Maltose to each 5 ounces.


Superior in sterility—a dry, stable powder
Easy to measure—almost instantly soluble
Meticulous quality control at every stage of manufacture

Dextri-Maltose

MEAD JOHNSON & COMPANY
Evansville 21, Ind., U.S.A.

MEAD

MEAD, JOHNSON & COMPANY, Suite 419 Eig Building, 8641 Coleville Road, Silver Spring, Maryland. JU 9-1222

CLINICAL PROCEEDINGS

OF THE CHILDRENS HOSPITAL

13th and W Streets, Washington 9, D. C.

Vol. IX *July 1953* No. 7

CONTENTS

HYPOTHYROIDISM IN INFANCY AND CHILDHOOD. *Sidney Rosenbaum, M.D., John Bunce, M.D.* 141

MANAGEMENT OF HYPERTHYROIDISM IN CHILDREN. *Allyn Griffin, M.D.* 144

THE ELECTROCARDIOGRAM IN ACUTE GLOMERULONEPHRITIS. *John O. Nestor, M.D.* 152

NIGHT TERRORS IN CHILDHOOD. *Robert B. Sullivan, M.D.* 157

CLINICO-PATHOLOGICAL CONFERENCE. *E. Clarence Rice, M.D., June Pollack, M.D., Bernice Wedum, M.D.* 162

EDITOR-IN-CHIEF
E. CLARENCE RICE, M.D.

MANAGING EDITORS
FREDERIC G. BURKE, M.D. SIDNEY ROSS, M.D.
JOSEPH M. LOPRESTI, M.D.

ASSOCIATE EDITORS
JOHN P. MCGOVERN, M.D. DAVID A. ST. MARTIN, M.D.
ROBERT H. PARROTT, M.D. MARSHALL C. SANFORD, M.D.
IRVING E. HALL, JR., M.D. ROBERT B. SULLIVAN, M.D.

GENERAL MANAGER
RHODA FRANCES DOBBIN

Contributing Editors from the Resident Staff: JOHN D. BUNCE, M.D.; BELINDA C. STRAIGHT, M.D.; JEAN D. LOCKHART, M.D.; MILTON S. GLATT, M.D.; H. E. C. MILLAR, M.D.; ARTHUR L. GOODRICH, M.D.; ALLYN B. GIFFIN, M.D.; AND ARDWIN H. BARSANTI, M.D.

Publications Committee of the Medical Staff: E. CLARENCE RICE, M.D.; THOMAS BRADLEY, M.D.; FREDERIC G. BURKE, M.D.; PRESTON A. MCLENDON, M.D.; ROBERT H. PARROTT, M.D.; SIDNEY ROSS, M.D.; HAROLD STEVENS, M.D., AND JOHN A. WASHINGTON, M.D.

PUBLISHED MONTHLY BY THE STAFF AND RESEARCH FOUNDATION OF THE CHILDREN'S HOSPITAL, WASHINGTON, D. C.

Cases are selected from the weekly conferences held each Sunday morning at 11:00 A.M., from the Clinico-pathological conferences held every other Tuesday afternoon at 1:00 P.M., and from the monthly Staff meeting.

This bulletin is printed for the benefit of the present and former members of the Attending and Resident Staffs, and the clinical clerks of Georgetown and George Washington Universities.

Subscription rate is $2.00 per year. Those interested make checks payable to "Clinical Proceedings Dept.," The Children's Hospital, Washington, D. C. Please notify on change of address.

Copyright 1953, Children's Hospital

Entered as second class matter November 21, 1946 at the post office at Washington, D. C., under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 538, Act of February 28, 1925, authorized January 17, 1947.

HYPOTHYROIDISM IN INFANCY AND CHILDHOOD

Case Report No. 266

Sidney Rosenbaum, M.D.
John Bunce, M.D.

INTRODUCTION

The diagnosis of hypothyroidism in infancy and childhood presents, at times, a challenge to the clinician where the more refined diagnostic methods are not always available. In these instances the history and clinical observation, before and after treatment, are the prime diagnostic criteria. This case is presented because it exemplifies the above points.

CASE PRESENTATION

B. C., a three-and-a-half-year old white female, was initially admitted to the Children's Hospital in June 1949, at which time she was 11 days old. The patient was the fifth child of a gravida 6, para 5 mother. The pregnancy was not supervised; however, the child was delivered at home by a physician. There was repiratory difficulty at birth and the physician told the mother that the child was abnormal. No further information was obtained relevant to that statement. The mother noted that the child had a "jaundiced" discoloration of the skin. The child was brought to the Children's Hospital for admission because of inability to feed and marked weight loss.

Family history revealed that there were four previous siblings all living and well and that the mother had a stillbirth in the seventh month of pregnancy following the birth of the patient. History of endocrine disorder was negative except that the mother stated that she was "nervous" throughout her pregnancy with the patient and that this state of "nervousness" was the cause of her subsequent stillbirth.

Physical examination at that time revealed a weak, lethargic, dehydrated and jaundiced infant. Routine laboratory studies in the hospital were essentially normal and roentgenogram of the long bones revealed normal bone age. No work-up for thyroid function was done. The patient was hydrated and then placed on a high protein, low fat formula which she took well. Good weight gain ensued. Following discharge from the hospital, the patient was followed up in the out-patient department for the next few months.

Developmentally she held her head up at 6 months, sat alone at one and a half years, walked at 2 years, and started talking at about the same time. Dentition started at 4 months. Her general health remained poor. She had frequent upper respiration infections, chickenpox, at 6 months, and for the first year of life had grand mal type seizures. The patient was noted to be slow, withdrawn, lethargic, inarticulate, fearful, and slept long hours. Physically the mother noticed the child's hair was coarse, and that she was quite obese.

At the age of 2 years the child was placed on 1 grain of thyroid daily. Following initiation of therapy, there was a complete cessation of most of the above features. However, treatment lasted only 6 months at the end of which time the child reverted to her previous state.

The second hospitalization was on July 9, 1952, with a chief complaint of increasing lethragy and anorexia. Physical examination at this time revealed an obese, pallid,

flabby mottling of the skin, infantile nasal-orbital configuration, doughy abdomen, dry skin and protruding tongue. The pulse rate was 100. There was a grade II high pitched systolic murmur at the apex with minimal transmission locally. The liver and spleen were both palpably enlarged. There was a slight diastasis recti. The child was uncommunicative, withdrawn, fearful and cried easily. Her head measured 19¾ inches, chest 22⅝ inches, and waist 22⅝ inches. She was 36⅛ inches tall, and her span was 34¾ inches. She weighed 36½ pounds.

The laboratory findings were as follows:

The hemogram revealed a hemoglobin of 5 grams, with a red blood cell count of 3.6 million; the white cell count was 6400 with a normal differential. The hematocrit was 19 per cent and the reticulocyte count was 2.1 per cent. The MCV was 51.5 cu. microns MCH was 13.6 micromicrograms, MCHC 26.5 per cent. Blood cholesterol was 162 milligrams per 100 milliliters and the alkaline phosphatase was 4.6 Bodansky units. Liver function tests were normal and a fasting blood sugar was 70 milligrams. A bone marrow examination revealed marked erythroid hyperplasia.

A roentgenogram of the chest revealed a slightly generalized enlargement of the cardiac silhouette while long bone films showed no evidence of dysgenesis and the bone age correlated well with the chronological age. A protein-bound iodine determination was 1.7 micrograms per 100 milliliters (control 5.2 micrograms per 100 milliliters.)

The child was placed on ¼ grain thyroid extract daily, together with supplemental iron, on September 20, 1952. Some response to therapy was noted clinically within two days, when the child's color had improved and she appeared more alert. Hemoglobin determination at this time was 6.8 grams.

During the remainder of her hospital stay the reticulocyte count rose to 10.9 per cent by September 30, and the hemoglobin increased to 9 grams. The child became increasingly alert, and showed some degree of initiative and communicability commensurate with her age. She was no longer irritable.

Thyroid medication was gradually increased until a maintenance dose of ¾ grain was achieved. At no time was there any evidence of drug toxicity.

At the time of discharge on October 22, 1952, she appeared alert and active with no overt evidence of retardation or irritability. Her appetite had improved perceptibly. The heart murmur which was present on admission had completely disappeared.

The patient was seen in the Endocrine Clinic 3 weeks later at which time progress was reported as satisfactory. Protein-bound iodine at this time was 3.2 micrograms per cent. The patient was continued on ¾ grain thryoid daily.

She was seen again on December 16, 1952, and not much change was noted objectively. She had not shown any significant growth and still weighed 36 pounds. Alkaline phosphatase was 7.4 Bodansky units and the hemoglobin had dropped to 4 grams. The dosage of thyroid extract was increased to 1 gram daily. When the patient was seen on February 17, 1953, we were impressed by the fact that she was less obese and her height had increased to 38 inches, an increase of 1⅞ inches.

DISCUSSION

This patient presented the following evidence of hypothyroidism:

(1) History of physical and mental torpor
(2) Physical findings of obesity, poor circulation, thick protruding tongue, doughy musculature, straight coarse hair, and dry skin, and coarse features interpreted as mongoloid in character
(3) Diminished protein-bound iodine

(4) Response to thyroid therapy
(5) Reversion to hypothyroid-like state upon cessation of medication
(6) Therapeutic clinical response, and increased protein bound iodine while on thyroid medication.

The clinical entity of hypothyroidism in infancy and childhood is variable. Depending on the time of onset, the degree of deficiency and interim treatments, a different picture will evolve. The ability of the laboratory to aid in the diagnosis has recently come to the foreground. In our patient, the finding of a low protein-bound iodine was the most conclusive evidence from a laboratory standpoint. The serum cholesterol may not be elevated and this eliminates the "therapeutic tests as applied to diagnosis" as suggested by Wilkins[1]. An increase in alkaline phosphatase with thyroid medication has been noted[2]. This occurred in our patient but not to a sufficient degree to be conclusive. The use of radioactive iodine uptake has brought to our armamentarium a more useful tool. A low uptake, however, is seen in other conditions and a high uptake has been reported in cretins[3]. In a study of radioactive iodine uptake curves by Lowery[4] et al., they reported diminished uptake in 4 cases including one which had been treated for about 3 years. A diminished response was seen in both primary and secondary hypothyroidism.

The determination of the protein-bound iodine is considered to be the most accurate measure of the activity of the thyroid gland. In the review on blood iodine by Rapport and Curtis[5] they cite evidence which confirms this statement. Peters and Man[6] believe the protein-bound iodine to be chiefly composed of thyroid hormone. The average normal value for protein-bound iodine as given by Talbot et al.[7] for children is 5.15 micrograms per cent. Danowski et al.[8] reporting on infants up to one year of age, point out that mean values differ within this age period and tend to approach values of older children and adults by the end of the first year. Talbot[7] reported values of 1.8–3.0 micrograms per 100 milliliters in 4 juvenile hypothyroid patients. Man[9] and her associates reported that the amount of protein-bound iodine in the blood of 9 cretins was less than 2 micrograms per 100 milliliters. In addition they have noted a correlation between the clinical response to thyroid therapy and the subsequent increase in protein-bound iodine.

REFERENCES

1. Wilkens; L.: *Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence.* Charles Thomas, 1950.
2. Talbot *et al.*: "Serum Alkaline Phosphatase as an Aid in Diagnosis of Cretinism and Juvenile Hypothyroidism," *A. J. Dis. Child.* **62:** 673, 1941.
3. Personal Communications.
4. Lowry *et al.*: "Radioactive Uptake Curve in Children," *Pediatrics* **4:** 627, 1949.
5. Rapport, R. H., and Curtis, G. M.: "The Clinical Significance of the Blood Iodine: A Review," *Journal of Clinical Endocrinology* **10:** 735, 1950.

6. Peters, J. P., and Man, E. B.: Cited by Rapport and Curtis.
7. Talbot, N. B., Bulter, A. M., Saltzman, A. H., and Rodrigues, P. M.: "The Colorimetric Estimation of Protein-Bound Serum Iodine," *J. Biol. Chem.* **153**: 497, 1944.
8. Danowski, T. S., Johnston, S. Y., Price, W. C., McKelvey, M., Stevenson, S. S., and McChisky, E. R.: "Protein-Bound Iodine in Infants from Birth to One Year of Age," *Pediatrics* **7**: 240, 1951.
9. Man, E. B., Culotta, C. S., Siegfried, D. A., and Stilson, C.: "Serum Precipitable Iodines in Recognition of Cretinism and in Control of Thyroid Medication," *J. Pediat.* **31**: 154, 1947.

MANAGEMENT OF HYPERTHYROIDISM IN CHILDREN*

Allyn Giffin, M.D.

Whenever thyrotoxicosis is seen in a child, conflicting opinions as to which form of therapy constitutes the best management of the patient are certain to arise. Few physicians have had extensive experience in the management of childhood hyperthyroidism, and conclusions are often drawn from experience with adults. With this in mind, it was felt that a review of the literature on the management of hyperthyroidism in children would be of interest.

Thyrotoxicosis is quite rare in children, constituting approximately one per cent of all hyperthyroid patients seen. It occurs in females seven times as frequently as it does in males[1]. The incidence increases around adolescence, at which time the thyroid begins to play a less important, and the gonads assume a more active role in body development. The underlying cause of this condition is not known, but the onset frequently follows an acute infection, psychic trauma, or endocrine imbalance, and there is a hereditary relationship demonstrable in some cases[2].

The symptoms of thyrotoxicosis in children are similar to those in adults, but certain differences are noted. The onset is usually gradual. Nervousness and emotional lability are the predominating early signs, and consequently these children are often treated as representing purely emotional problems. As the disturbance becomes more severe, other symptoms appear, such as loss of weight, or failure to gain weight in spite of voracious appetite, heat intolerance, difficulty in school work, vomiting and diarrhea. The subjective complaints such as palpitations, dizziness and weakness, which are common in adults, are seldom seen in children.

The presenting complaint is often "swelling of the neck" or "bulging eyes". The enlargement of the gland is usually of a diffuse nature. Adenomatous goiter is rarely the cause of thyrotoxicosis in children[2]. Exophthalmos is present in over 60 per cent of these children, and is often associated with lid lag and other ophthalmoplegias. Tremor is a late develop-

* Acknowledgment is made of the assistance of Dr. John Washington, for his consultation; Mr. Samuel Sanchuck of Walter Reed Army Hospital, for the protein-bound iodine determination; and Dr. Monty Greer of the National Institutes of Health for consultation and for radioactive iodine uptake determination.

ment and is often not present at the time of diagnosis. These children are frequently tall for their age, and are usually quite slender. The skin is typically warm and moist. Tachycardia is usually present and there is an increase in the blood pressure and the pulse pressure. The disease is not usually as severe in children as in adults, and a thyrotoxic crisis is very rare.

The laboratory may be of considerable aid in the diagnosis and management of hyperthyroidism. A brief discussion of the pertinent procedures is presented[2-6]:

1. *Basal Metabolic Rate:* this is usually increased above +20 and often above +40. Considerable difficulty is encountered in carrying out the procedure in young children, and a well trained technician is necessary.
2. *Fasting Serum Cholesterol:* this is usually decreased but these results are not reliable. The normal level is 150–220 mg per 100 ml.
3. *Urinary Creatine–Creatine Ratio:* usually there is an increased excretion of creatine as creatine and less as creatinine. It is necessary for the child to be on a creatine free diet for 3–4 days before the test is run and a 24 hours urine sample must be collected. The normal level is 10–30 per cent. In hyperthyroidism a level of 30–65 per cent will often be found.
4. *Radioactive Iodine Uptake:* a calculated dose of I^{131} is given by mouth and the percentage taken up by the thyroid gland is determined by a Geiger counter. Trained personnel are obviously necessary for this test. It is considered to be quite accurate. A normal gland will absorb 10 to 40 per cent. Above 50 per cent uptake is considered to be pathognomonic of hyperthyroidism.
5. *Protein Bound Iodine:* this is probably the most accurate method of determining thyroid activity. It is however, quite difficult to do. Normal is 4 to 8 gammas/100 ml. This is increased in hyperthyroidism.
6. *Skeletal Maturation:* this is best determined by X-rays of the carpal bones and there is usually an increase in the bone age of the patient with hyperthyroidism. Because of the slow changes that take place in bones, this is of little use in management of the patient.

CASE PRESENTATION*

C. D. was a seven-year-old colored girl admitted to Children's Hospital with a chief complaint of choking at night. She had been in good health until one year prior to admission when she began to lose weight. A few months later the mother noticed that she was becoming quite nervous and was easily upset. She would be happy one minute and crying the next. Four months before admission her eyes became more prominent. The mother further volunteered the information that the child was always complaining of heat and that she itched a great deal. Her appetite had increased

* This patient was on the ward service of Dr. William Anderson.

tremendously during the past year. A swelling in her neck had been noticed for the past four months. All of these symptoms had been gradually increasing in severity until admission. During the week before admission she had awakened nightly and complained of a choking sensation; this was relieved by drinking water or by being reassured.

This child had done well in school during the previous year; however, this year she had been a behaviour problem and had been getting poor grades.

She had had no serious illnesses or operations. Her birth and development had been normal and her diet adequate.

There were no known endocrine disorders in her family. The mother had never heard of the terms thyroid or goiter. The mother, father, and four siblings were all living and in good health.

Physical examination revealed a tall, asthenic, nervous seven-year-old colored female in no distress who moved constantly during the examination. Her pulse was 148 per minute, respirations 30 per minute and blood pressure 150/50. She weighed 46 pounds and her height was 51 inches. Her skin was warm, soft and moist. There was no evidence of lymphadenopathy. Her eyes showed a moderate exophthalmos bilaterally (20 millimeters in both eyes) and there was some difficulty with convergence, but no lid lag or other ophthalmoplegia. The ear, nose and throat examination was negative. A diffusely enlarged thyroid gland was approximately twice normal size. No thrills or bruit was heard, but a venous hum was present over the right lobe.

The heart was slightly enlarged and a diffuse apical beat was seen and felt. There was a tachycardia with a normal rhythm. No murmurs were heard on auscultation. The lungs were clear to percussion and auscultation. The abdomen was soft and no masses or organs were palpable. There was a fine tremor of both hands. The genitals were normal. Neurological examination was entirely negative except for an increase in deep tendon reflexes.

Laboratory studies that were done included complete blood counts, urinalysis, serologic studies for syphilis and a sickling preparation, all of which were negative. A fasting serum cholesterol was 140 mg per 100 ml. Three basal metabolic rates were done and were reported as +28, +28 and +27. Her radioactive iodine uptake was 104 per cent in 24 hours, and protein bound iodine was 21 gammas per 100 ml.

Roentgen rays examination of the chest showed no evidence of abnormality. The heart was of normal size and contour. There was no evidence of a substernal thyroid gland. The bone age was 7 years 10 months [6] and chronological age was 6 years 11 months. The skull plates showed no abnormality and the sella turcica and clinoid processes were normal. An electrocardiogram showed a sinus tachycardia but no other abnormalities.

The child was in the hospital for fourteen days while studies were being done and was kept on absolute bed rest. Her pulse varied between 100–150 per minute. Her blood pressure varied from 118 to 150 systolic and 20 to 50 diastolic. Her hospital course was uneventful. She was started on prophylthiouracil in a dose of 100 mgms every 8 hours while in the hospital and has continued on that dose at home.

She has been seen in the Endocrine Clinic on several occasions since discharge. The last time was three months following discharge at which time her toxic symptoms had cleared and it was felt that she was in a euthyroid state. The emotional instability, nervousness and tremor of the hands had all cleared. She was sleeping well and was not as easily fatigued. She had been back in school for two weeks and had been doing well. The apical thrust had diminished. Her pulse was 88 per minute and her blood pressure was 100/70. The thyroid gland was approximately the same size. The

exophthalmos was essentially the same (21 mm in both eyes). The blood count had remained entirely normal except for an eosinophilia of 7 to 9 per cent.

Our plan at present is that she be continued on propylthiouracil (100 mgms every 8 hours) and to be followed closely by physical examination and periodic protein bound iodine determinations.

DISCUSSION

The physician has a choice of three methods of treating hyperthyroidism i.e. medical, surgical, or irradiation. Regardless of what method of treatment is used the patient must be evaluated as an individual and not as a hyperactive gland. A precipitating cause must be searched for and removed. Any coexisting infection should be treated, an attempt to relieve emotional and environmental infection should be made, and nutritional deficiencies should be corrected with a good nutritional status maintained. A social worker's evaluation of the home and parents will be of aid in determining the type of treatment to be used. Psychiatric evaluation and treatment may be indicated. As in any other chronic disease, both the parents and the child should be informed about the nature of the disease and what is to be expected with therapy. During the period of evaluation and early therapy, the child should be kept at bed rest, sedated, and given a high caloric diet. The child should be allowed to gradually increase activity only after showing signs of coming under control and should not be allowed to return to school until considered to be in a euthyroid state. These general principles must be followed no matter which method of therapy is pursued.

Irradiation

In the past, roentgen therapy was found to be of benefit in the control of patients with hyperthyroidism[7]. This method has not been used extensively and in recent years has been entirely replaced by the use of radioactive iodine. Much work has been done with radioactive iodine and very good results have been reported by this method of treatment[8-11]. However, most of the cases reported are adults and almost all of the children who have been treated with I^{131} have been in the adolescent age group. As a consequence, the value of I^{131} in younger children is still somewhat speculative.

The advantages of using I^{131} are:

1. It is a safe procedure when done by trained personnel and has a high percentage of remissions,
2. Complications other than hypothyroidism are rare. No laryngeal paralysis or hypoparathyroidism occur as in surgical removal,
3. Further therapy can be given easily if the patient has not been controlled by the initial dose.

The disadvantages to this method of treatment are:

1. It is difficult to judge the size of the dose and a significant percentage develop hypothyroidism,
2. The damage done to the thyroid is completely irreversible,
3. The possibility of other glandular disturbances secondary to thyroid suppression or the effect of I^{131} on the other endocrine glands which may interfere with normal growth and development are theoretical possibilities,
4. There is a possibility of a carcinogenic action of radioactive iodine

Surgical Therapy

The surgical management of hyperthyroidism is a time-tested, effective method of therapy. A marked decrease in the mortality rate has been accomplished over the past thirty years due to a general improvement of surgical technique, the introduction of iodine and later the thiourea derivatives into the pre-operative management. Many feel, in spite of marked advances in medical therapy, that surgery is still the treatment of choice in hyperthyroidism[12-15]. The advantages of surgery in these cases are:

1. A prolonged period of treatment is not necessary,
2. The percentage of cure is very high,
3. There are conditions which, of themselves, are positive indications for surgery[12, 16, 17]:
   a. Chronic thyroiditis,
   b. Substernal or intra-thoracic thyroid,
   c. Uninodular or large multinodular goiter,
   d. Failure to respond to medical therapy, toxicity of drugs, or a persistently large gland in spite of medical therapy.
   e. If it is felt that the patient will not cooperate for the long period necessary for medical therapy.

The disadvantages of surgery are significant enough to indicate that there is still room for improvement. These are:

1. A mortality rate even in good hands of 2.5 per cent in children,
2. The significant number of children who have a recurrence of hyperthyroidism, develop hypothyroidism, hypoparathyroidism, or other endocrine disturbances, following surgery[7, 18-20].

Medical Therapy

To control the symptoms of a thyrotoxic child, without the removal or destruction of the thyroid gland, has long been the goal in this disease. The importance of this gland in normal growth and development during the prepubertal period makes it necessary that we approach thyrotoxicosis in children more conservatively than we would in adults. As Topper[18],

McIntosh[19], and Kumstader[20], have pointed out, anything that would cause even temporary remissions of symptoms of hyperthyroidism until puberty is established would be very advantageous.

Even before the development of the thiourea compounds, many attempts to control the symptoms of thyrotoxicosis by conservative means were attempted. Reilly[7], in 1940, reported a group of thirty children with hyperthyroidism of whom fifteen were controlled by purely medical means (rest, diet, sedation and occasionally iodine), and concluded, "that in half of the cases thyroid hyperplasia is relatively benign, self limited, short lived, and not a great menace to health in childhood or later in life."

With these thoughts in mind, many clinicians greeted the development of thiouracil and its derivatives as the answer to thyrotoxicosis in children, and several reports of series of cases treated with these drugs are now in the literature[21-30].

There are, at present, two groups of drugs available for treatment i.e. thiouracils and imidazoles. Their action in suppressing thyroid function is by depressing the oxidative enzyme systems through which inorganic iodine is bound to protein to form thyroid hormone. There is no suppression of the thyrotropic hormone of the anterior pituitary, and there results a hypertrophy, hyperplasia, increased vascularity and decreased storage of colloid in the thyroid[16].

Of the thiourea drugs that have been used, thiouracil is now considered too toxic for further use. Itrumil, propylthiouracil and methylthiouracil are reported to be of approximately equal toxicity. The toxic reactions of these drugs are not frequent (1.8 to 2 per cent)[15], and are usually of a mild, transient nature, such as skin rash or fever. Eosinophilia of 8 to 15 per cent is noted quite frequently[22]. Granulocytopenia[31] and agranulocytosis[32, 33], have been reported but these complications are quite rare. Of these drugs, propylthiouracil is probably the most effective.

After therapy with propylthiouracil is started, two to three months are necessary before the patient becomes completely asymptomatic but improvement is noted much earlier. Treatment should be continued for at least one year and then tapered off gradually. If symptoms recur at the end of this course, another period of treatment of 6 to 12 months should be given. Propylthiouracil does not usually decrease the exophthalmos and the size of the gland will often increase in size early in the treatment. Iodine should not be used as an adjunct to the thiourea compounds except preoperatively, since a much larger dose would be necessary to control the patient.

Thyroid extract started cautiously in doses of 15 to 30 mgms daily after the patient is asymptomatic may, by suppression of the thyrotropic hormone, result in a decrease in the size of the gland, and a decrease in the

exophthalmos[23]. If the goiter is not very large and the exophthalmos is not great, no additional therapy will be necessary since prolonged use of propylthiouracil often causes a decrease in both the size of the gland and the exophthalmos[20].

The dose of propylthiouracil should be quite high ranging from 300 to 500 mgms daily. Since this drug is rapidly excreted, it is necessary to maintain a relatively rigid schedule, giving one-third of the daily dose every eight hours. When the patient becomes euthyroid, the dose may be gradually cut to a daily maintenance of 100 to 300 mgms. Rather than decreasing the dose of propylthiouracil, it is probably better to give thyroid extract when mild hypothyroid symptoms develop. This continues the complete suppression of the gland during the course of treatment and at the same time keeps the patient in a euthyroid state.

The most common reasons for recurrence of symptoms while on therapy or after a course has been completed are[20]:

1. Too small a dose of propythiouracil,
2. Too short a period of therapy,
3. Too much thyroid extract,
4. An acute infection,
5. An emotional shock.

If the reasons for failure of therapy are kept in mind and the patient is closely observed while under therapy, a remission rate of 65 to 75 per cent after one course of treatment, and as high as 85 per cent after an additional course can be expected[28, 30]. How long the patient will remain in remission cannot be stated with certainty. However, cases have been reported as having complete remissions from 3 to 4 years after therapy was discontinued. It is not being overly optimistic to expect a high percentage of complete remissions and to be able to control most of the remaining patients until puberty is established.

Results of treatment with the imidazole drugs have recently appeared in the literature[26-27]. Methimazole (Tapizole) is a much more potent drug and brings the patient under control more rapidly than propylthiouracil. However, the dose in children, the duration of therapy and the long term toxicity have not been thoroughly evaluated at this time. It is too early to draw any conclusions about the effect of other imidazole drugs.

CONCLUSIONS

In deciding what form of treatment to use in childhood thyrotoxicosis, each patient must be evaluated individually. There are certain positive indications (see above) where surgery is the only form of therapy to consider.

The status of radioactive iodine in the treatment of children with hyper-

thyroidism is still somewhat uncertain. Until some long term follow-up reports are available it is probably better to use one of the other therapeutic approaches.

If there are no positive surgical indications present and if it appears that the patient will cooperate, we feel that most children with thyrotoxicosis deserve a prolonged trial on a medical regimen before resorting to surgery. Many children can be expected to have permanent remissions and others can be carried to puberty by medical management alone.

Of the thyrogenic drugs available, propylthiouracil is probably the drug of choice at this time for the long term management of childhood hyperthyroidism. It has a very low toxicity and will bring about remissions in the vast majority of patients with this disease.

General medical management still plays an important role in the treatment of a child with hyperthyroidism.

REFERENCES

1. Kennedy, R. L.: The Thyroid Gland, in Brenneman's *Practice of Pediatrics*. Prior, Vol. I, Chap. 38, 1940.
2. Wilkins, L.: *Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence*. Thomas, 2nd Ed., 1950.
3. Warkany, J.: Disorders of the Thyroid Gland, in *Mitchell-Nelson Textbook of Pediatrics*, 5th Ed., P. 1382 W. B. Saunders, Co., Philadelphia and London.
4. Werner, S. C.: Laboratory Procedures in the Diagnosis of Hyperthyroidism. Postgrad. Med., **8**: 511, 1950.
5. Schlesinger, B.: Accelerated Skeletal Development from Thyrotoxicosis and Thyroid Overdosage in Childhood. Lancet, Aug. 1951, P. 289.
6. Todd, T. W.: *Atlas of Skeletal Maturation*. C. V. Mosby, Co.
7. Reilly, W. A.: Thyrotoxicosis. Am. J. Dis. Child., **60**: 78, 1940.
8. Forbes, G. B., and Perley, A. M.: Treatment of Hyperthyroidism with Radioactive Iodine. J. Pediat., **38**: 158, 1951.
9. Miller, E. R. et al.: Studies with Radioiodine; II Treatment of Patients with Hyperthyroidism by I-131, Radiology, **57**: 227, 1953.
10. Soley, M. H., and Miller, E. R.: Treatment of Graves' Disease with Radioactive Iodine. M. Clin. North Am., **32**: 3, W. B. Saunders, Co.
11. Gordon, E. S., and Albright, E. C.: Treatment of Thyrotoxicosis with Radioactive Iodine. A.M.A., **143**: 1129, 1950.
12. Jackson, A. S., and Haley, H. B.: Exophthalmic Goiter in Children: Treatment with Propylthiouracil, Am. J. M. Sc., **218**: 493, 1949.
13. Bartels, E. C.: Appraisal of Goiterogens: Results of Treatment with Thiouracil, Propylthiouracil and Related Antithyroid Drugs. J. Clin. End., **8**: 766, 1948.
14. Bartels, E. C.: Hyperthyroidism in Children. Lahey Clin. Bull., **6**: 68, 1949
15. McGavack, I. H.: The Use of Antithyroid Drugs in Hyperthyroidism. M. Clin. North Am. May 1952, P. 603, W. B. Saunders, Co.
16. Williams, R. H.: Selection of Therapy for Individual Patients with Thyrotoxicosis J A. M. A., **139**: 1064, 1949.
17. Topper, Ann: Treatment of Exophthalmic Goiter in Childhood. Am. J. Child., **76**: 26, 1948.
18. McIntosh, C. B.: Treatment of Hyperthyroidism in Children J. Pediat., **25**: 133, 1944.
19. Kumstader, R. H., and Stein, A. F.: Treatment of Thyrotoxicosis in Children with Thiourea Derivatives. Ped., **6**: 244, 1950.
20. Burke, F. G.: Thyrotoxicosis in a Child Managed with Thiouracil. Clin. Proc. Child. Hosp., Washington. D. C., **2**: 129, 1946.
21. Williams, L. P., and Jamey, F. R.: Thiouracil in Childhood Hyperthyroidism. J. Pediat., **30**: 370, 1947.
22. Drake, M. E. et al.: Treatment of Juvenile Thyrotoxicosis with Propylthiouracil. Am. J. Dis. of Child., **82**: 43, 1951.
23. Crile, G., Jr., and McCullagh, E. P.: Treatment of Hyperthyroidism with Thiourea Derivatives. Annals of Surgery, **134**: 18, 1951.

25. Astwood, E. B., and Vander Laan, W. P.: Thiouracil Derivatives of Greater Activity for the Treatment of Hyperthyroidism. J. End., **5**: 428, 1945.
26. Taylor, M. et al.: Treatment of Thyrotoxicosis with Methimazole. Am. J. of Med. Sc., **222**: 138, 1951.
27. Irwin, H. D. et al.: Propylthiouracil and Methimazole Therapy. J. A. M. A., **149**: 1952.
28. Rose, E., and Shorey, J. M.: Late Results in Treatment of Thyrotoxicosis with Goiterogenic Compounds. J. Clin. End. **11**: 507, 1951.
29. Greenberg, and Bruger: Observations on the Prolonged Medical Management of Toxic Diffuse Goiter with Thiouracil and Propylthiouracil. Am. J. M. Sc., **220**: 373, 1950.
30. Iversen: Late Results from Continuous Treatment of Thyrotoxicosis with Methylthiouracil. J. Clin. End., **11**: 297, 1951.
31. Davis H., Jr., and Murphy, F. J.: Leukopenia and Drug Fever in Juvenile Hyperthyroidism Treated with Propylthiouracil. Clin. Proc. Child. Hosp., Wash., D. C., **5**: 286, 1949.
32. Levingston, H. L., and Levingston, S. F.: Agranulocytosis and Hepatocellular Jaundice: Toxic Reactions Following Use of Propylthiouracil. J. A. M. A., **135**: 510, 1947.
33. Juliar, B., and Harris, J. L.: Fatal Agranulocytosis Occurring During Propylthiouracil Therapy: Report of a Case. J. A. M. A., **139**: 646, 1949.

THE ELECTROCARDIOGRAM IN ACUTE GLOMERULONEPHRITIS

Special Report No. 267

John O. Nestor, M.D.

INTRODUCTION

Although it has been known and recorded in medical literature for years that certain abnormalities occurring in the course of acute glomerulonephritis will show up on the electrocardiogram, few good examples have been published recently. The paucity of such published illustrations since the adoption of the standard twelve-lead electrocardiogram including the unipolar limb and chest leads has led to the presentation of the following case.

CASE PRESENTATION

A five-and-a-half year old white girl was admitted to Children's Hospital, Washington, D. C., on April 17, 1953, because of swelling of the eyelids and abdomen for five days. About four weeks prior to admission she had contracted a bad cold from which she had fully recovered several days before the onset of the present illness. There were no other signs or symptoms except a slight oliguria.

The family history indicated the presence of allergy and diabetes in the immediate family. The past history revealed only that the child seemed allergic to certain foods and had frequent respiratory infections. An x-ray examination made of the chest in 1951 because of a chronic cough showed only increased broncho-vascular markings and a heart normal in size.

Examination on admission revealed a well-developed, well-nourished white girl, whose temperature was normal. There was a 2 + pretibial edema, but no periorbital edema. The systolic blood pressure was 140 mm Hg. The abdomen was distended and tympanitic and the liver extended two fingerbreadths below the costal margin. The optic fundi were normal.

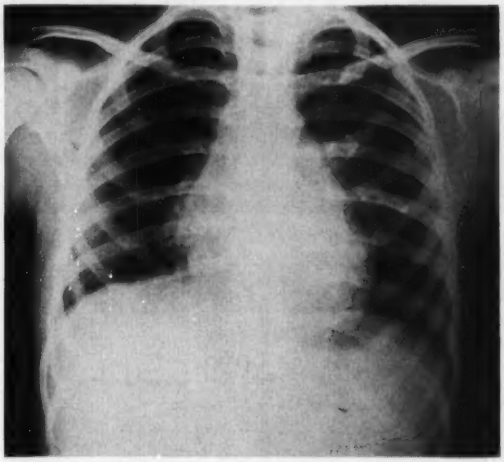


FIG. 1. Roentgenogram of chest made in 1951, showing heart normal in size, but increased bronchovascular markings.

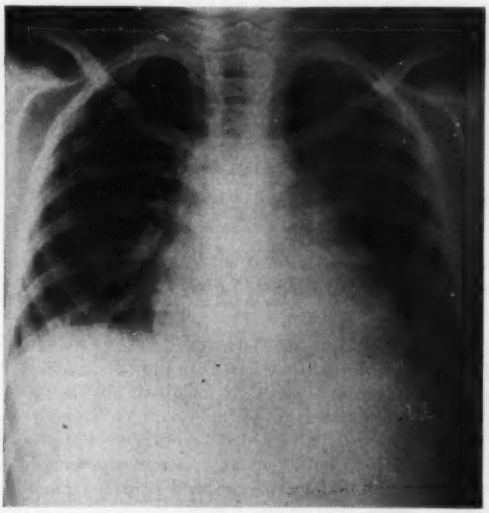


FIG. 2. Cardiac enlargement and pulmonary congestion shown by teleroentgenogram taken April 18, 1953.

The day after admission the patient became drowsy and vomited once. The blood pressure remained elevated. A teleroentgenogram indicated cardiac enlargement and

pulmonary congestion. The urine analysis revealed 50 mgm/100 ml albumin but no red cells. The blood count disclosed a moderate anemia and slight leukocytosis with a normal differential leukocyte count.

On the third hospital day (April 20, 1953) although there was only a trace of albumin in the urine, between 5 and 10 red blood cells per high power field were reported. The edema had almost disappeared. The sedimentation rate was 23 mm/hr and the NPN and BUN were both normal. The blood pressure was still elevated. A slight soft systolic murmur could be heard along the lower left sternal border and out to the apex. No thrills or shocks were present and P2 was normal.

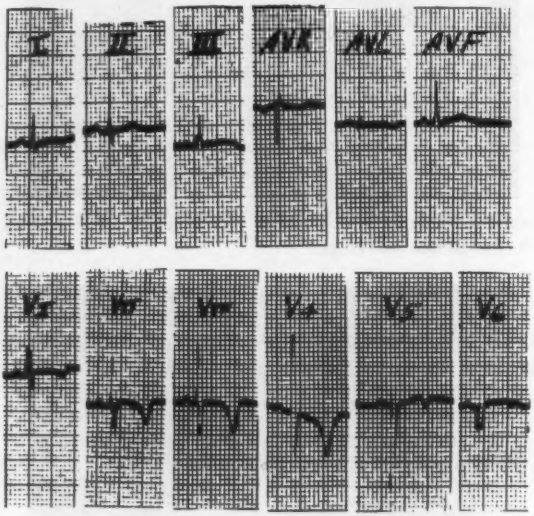
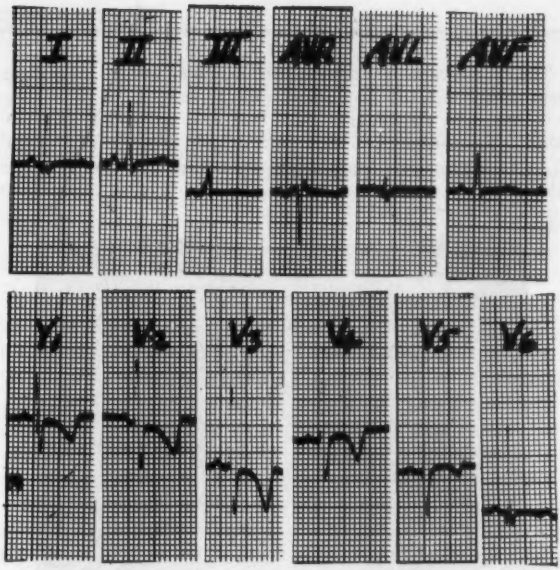


FIG. 3. Electrocardiogram taken April 20, 1953, showing inverted T in Leads I and AVL, and Diphasic T in Leads AVR, V_5 and V_6.

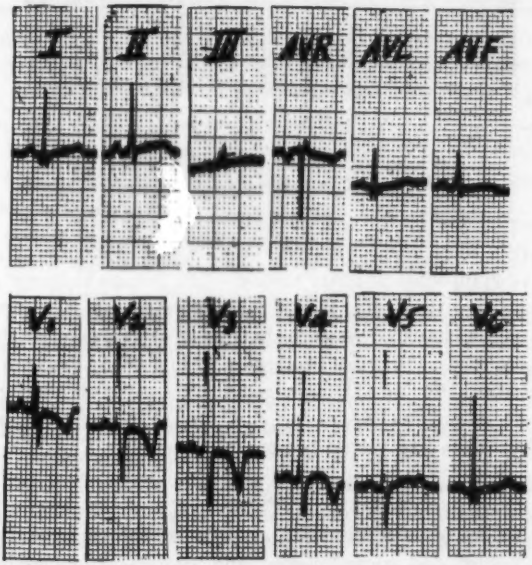
The electrocardiogram revealed a normal sinus rhythm at the rate of 80 per minute with a balanced axis and a semi-vertical heart with PR, .13 seconds; QRS, .07 seconds; and QT, .36 seconds. T waves were generally low in all limb leads, inverted in leads I, AVL, V_1 through V_4, and diphasic in AVR, V_5, and V_6. There was an RSR′ in V_1. These changes definitely indicated myocardial abnormality. Fluoroscopy with barium swallow revealed enlargment of both ventricles, being most marked on the left. The left auricle was not enlarged and there were no abnormal retroesophageal vessels. There was a left-sided aortic arch, and somewhat increased pulmonary vascularity, but no hilar pulsation.

The course in the hospital was relatively uneventful. Within a few days the blood pressure returned to normal, the edema albuminuria and hematuria disappeared, and the child was discharged on April 29, 1953, to convalesce at home.

By June 1, 1953, the heart had diminished in size and was within the upper limits



FIGS. 4 and 5. Improvement shown by electrocardiogram taken June 1, 1953 (above) with low upright T in Leads I and AVL and Diphasic T in Leads V_5 and V_6.



Return of the electrocardiogram to normal on July 6, 1953 (below) with normal upright T in Leads I and AVL and upright T in Leads V_5 and V_6.

of normal. The electrocardiogram had assumed more normal appearance and the urinalysis was negative.

On July 6, 1953, the electrocardiogram had returned to normal, the heart was normal in size on fluoroscopy, but the sedimentation rate was still slightly elevated (26 mm/hr). A roentgenogram taken a few days later indicated that the heart was normal in size.

FIG. 6. Roentgenogram taken in July, 1953, indicating return of heart to normal.

DISCUSSION

The abnormalities in the electrocardiogram associated with acute glomerulonephritis may occur independently of the presence or absence of other signs or symptoms of heart disease even though they are more commonly associated with cardiac failure and hypertension. The most striking and characteristic changes consist of flattening or inversion of the T waves in one or more leads. Other less common findings mentioned in the literature are prolonged PR and QT intervals, and transient changes in the mean electrical axis, minor changes in the P waves, QRS complex, and ST segments. Arrhythmias are rarely present.

SUMMARY

The case report of a patient with acute glomerulonephritis complicated by cardiac failure and hypertension, and showing the classical electrocardiographic changes, has been presented.

REFERENCES

1. Ash, R., Rubin, M. I., and Rapoport, M.: Electrocardiographic Variations in Acute Glomerulonephritis. Am. J. Dis. Child., 67: 106, 1944.
2. Rubin, M. I., and Rapoport, M.: The Three Major Complications of Acute Hemorrhagic Nephritis in Children. Penn. M. J., 40: 1029, 1937.
3. Rubin, M. I., and Rapoport, M.: Cardiac Complications of Acute Hemorrhagic Nephritis in Children. Am. J. Dis. Child., 55: 244, 1938.
4. Whitehill, M. R., Longcope, W. T., and Williams, R.: The Occurrence and Significance of Myocarditis in Acute Hemorrhagic Nephritis. Bull. Johns Hopkins Hospital 1939, LXIV 83.

NIGHT TERRORS IN CHILDHOOD

Case Report No. 268

Robert B. Sullivan, M.D.

INTRODUCTION

Night terrors (Pavor Nocturnus), while a source of alarm and anxiety to parents of the affected child, can in most cases be easily managed by the pediatrician. The child screams in terror at night; he cannot be comforted and even seems unable to recognize his parents. Such disorientation, with visual or auditory hallucinations, suggests to the child's parents a severe mental illness. To the pediatrician, however, it indicates an emotional problem arising out of certain stages in the child's development.

Night terrors are less frequent than nightmares. The age range of children affected is from one to 13 years, with the symptoms occurring most often in children between the ages of 3 and 6 years.

At the root of the problem is one basic fear: That of physical hurt. In the very young, this stems from the infant's growing awareness of his separateness from his mother. Coupled with this realization of self-sufficiency, is a feeling of vulnerability—the loss of a certain sense of protection afforded by the earlier relationship. This basic fear may also arise from expressed or implied disapproval by a parent for forbidden behavior.

In the 3 to 6-year-old age group, development has progressed to the point where the child begins to experiment in ways of relating himself to his parents. He discovers ways in which he can monopolize the attention of one parent and eliminate the other parent from this relationship. His fear of bodily injury can now be connected with his fear of retaliation on the part of the excluded parent.

Factors which intensify the feelings mentioned above, and precipitate night terrors, include: opportunities to see, hear or fantasize sexual activity between parents; surgery (tonsillectomy, circumcision, appendectomy); illnesses; traumatic events (such as attack by a dog); and stories of agression and mutilation.

Both prevention and treatment of night terrors are dependent on attention to parental attitudes about sexual and aggressive activity, as well as to the precipitating factors.

CASE PRESENTATION

M. C., a white girl of four years and five months, was referred to the psychiatric clinic because of night terrors.

The mother, a rather solemn but attractive young woman of 23 years, was interviewed first. She reported that two weeks previously, without any forewarning, the child awoke at 3 a.m., screaming that there were bugs in her bed, on the floor, walls and ceiling. She was "like a mad person," and the parents were unable to comfort her by voice or touch. She was moved into the parents' bed and continued screaming, saying that there were bugs there also. She could not bear to have the bed covers over her. Her screaming continued until dawn, when it was found that the child had no fever or signs of physical illness.

During the day the child looked off into space and did not play well. When the mother went into the bedroom, the child followed her and looked in apprehensively. She took no nap. While sitting on the toilet, the child thought she saw a bug on her sleeve, but it proved to be a black thread. At 8 p.m. the child went to sleep on the living room sofa and was then moved to her bed, where she slept until morning. The next night, however, the terrors recurred, continuing in a similar fashion every other night up to the time the mother came to the clinic.

While both parents were understandably upset, confused, frightened and tired, these episodes seemed to have no effect on a young brother, aged 3 years and one month.

All of the family were sleeping in the same room, the parents in a double bed and the children in single beds. The family shares a house with another family and although there is a bedroom for the children, they were moved in with the parents because of the possibility of their getting up early in the morning and disturbing the other sleepers. This had been the arrangement since the other family moved into the house three months previously. From the age of 6 months up to this time the child had slept in her own room, having no difficulties or disturbances.

Patient's History

The child's early history is a remarkably uneventful one. Although she was born after several episodes of false labor, she was a healthy infant. Stages in her development, up to the time the patient's mother brought her to the clinic, had presented no problem. Both this child and her brother, who was born when the patient was 16 months old, were extremely easy to manage until the present illness.

At the time her brother was born, the patient went to stay with her paternal grandparents, remaining with them for a month. During this time she had the measles and after returning home, she had mumps. She has had no injuries or surgery.

She is an affectionate child and requires a good deal of loving, but has always been quiet and shy. She will mildly pinch her brother when she is angry, but shows no jealousy, and the parents show no favoritism. She has previously been more openly affectionate towards her father. Since her present illness, however, the child has become rather distant from the father and has turned to the mother for what little affection she now seeks.

The patient and her brother like to play at keeping house. In their game, which they call "honey," he is the father and she the mother. No negative feelings are

ever worked out in their play. This may be due to the fact that the parents have tended to suppress any negative expression, characterizing it as "not nice."

The patient has evinced a normal interest, asking questions about her body, but less often than her brother does. She has asked about her brother's genital organ, being told by her mother that God made him that way. She asked where babies come from and was told that God sent them. She inquired, "Where was I before I was born?" and her mother told her that she was not old enough to know.

Interview with Parents

The patient's mother was somewhat uncomfortable in discussing her own family background. She said that her parents fought bitterly and her home life was unhappy. She is determined that there will be no strife or unpleasantness in her home. She is, however, resentful that because of the difficulty of both births, her doctors advised tubal ligation to prevent further pregnancies

The father was also interviewed. He proved to be a quiet, solemn, rather reticent man of 28 years. He was well dressed and had a rather frozen-faced, depressed look which softened somewhat during the discussion. He thought that he had been away at work too much recently. He also expressed a feeling of guilt about having spanked the patient during the first episode of night terror.

He believes that he does not allow the children to express negative feelings, but has not had to openly suppress them very much. The patient has shown no sexual concern to him, so far as he remembers, and he believes that he would not be upset if she did. She has asked if a woman has a "bottom." The father did not know what she meant and had forgotten his reply.

Interview with Patient

The interviewer met the child in the waiting room where she was seated next to her father. She was well-dressed and clean. Her solemn and frozen expression seemed to mirror that of her father. When the child was invited into the play-room she came in without any sign of emotion and without a backward glance.

The child was obviously uncomfortable in this new situation, however, and was unable to initiate any play activity until she felt reassured. While she refused the offer of a doll baby, she did accept a water pistol offered her by the interviewer. She was invited to shoot at the doll house where a family of plastic dolls had been arranged beforehand. With no hesitation and with evident enjoyment, she shot the father, the mother, brother, and girl dolls.

By this time the patient was much more relaxed and began to talk freely, apparently trying to confide in the interviewer. She made several unrelated remarks, such as "Daddy said to go to bed and think about chickens. I thought about nuts." When the interviewer inquired, "You thought about nuts?", she replied, "We don't eat them." The interviewer then asked the child if she were thinking about nuts because she dreamed. The child replied in the affirmative, but became tense, and was unable to describe her dreams, as if the subject were too unpleasant.

While she seemed friendly and interested, the child was disturbed by proximity either of people or of objects. She not only acted uncomfortable with nearness to the examiner, but also was very careful in playing with the dollhouse and dolls to isolate each piece of furniture. She also was very conscious of and concerned about disorder or messiness.

Her interest in body form and its relationship to her aggressive feelings was shown in several indirect ways. The child turned to the water pistol again. In the course of

the shooting, the interviewer purposely shot a male doll in the gluteal region calling it the "bottom." The child laughed, taking the male doll and shooting it pointedly in the genital region.

She also enjoyed making snakes out of clay and shooting them with a water pistol. She enjoyed playing with the typewriter and the sewing machine and tried to operate them. She also liked taking things apart to see what made them work and she liked to look into closed places.

Her concern with family relationships was evidenced in several remarks she made about her brother whom she called "my baby boy." Her attempt to fix family relationships in her mind was shown by such remarks as "His name is Johnny; he's my brother and I'm his sister."

Altogether, the child was an attractive, healthy little girl with good coordination and with the normal urges for one of her years. The outstanding feature pointed up by the interview was her need to be well controlled, because of her feeling that aggressive or messy activities would be unacceptable.

DISCUSSION

In formulating the emotional factors responsible for the upset condition of this child, certain deductions can be made on the basis of the evidence at hand, since we have a rather sound body of knowledge describing the emotional problems to be met by the child in the 3 to 6-year age group.

During this period the child attempts to form workable concepts of birth and death, parent and child, love and hate. He also begins to experiment with sexual feelings in something approaching the adult genital form. The child also experiments with the idea of monopolizing the attention of one parent and excluding the other. These attempts are recognized by the child as being unacceptable to the excluded parent and suggest to him the possibility of retaliation. Since he cannot control his urges and he cannot bear the thought of the parent's disapproval or retaliation for these forbidden desires, the child distorts them into other forms in partial solution of the conflict.

We know that in the case at hand neither parent is comfortable with the direct expression of negative feelings. By expressing their disapproval, they have succeeded in curbing any aggressive outlet the children might employ for such feelings.

We also know that the birth process for the mother had been so traumatic that two doctors advised tubal ligation to prevent pregnancies. The separation of the child from her mother for over a month at the time the patient's brother was born, was complicated by the child's having the measles and the mumps. All this suggests that the child may have associated a considerable amount of unpleasantness with the birth process. This association would arise not only from the atmosphere communicated to the child by her parents, but also from the child's own discomfort during the time that her mother was away at the hospital.

We also know that the child's tendency was to conform. Until the advent of the present illness, she had apparently found conformity the most satisfactory way of relating herself to her parents, being very uncomfortable at any feeling of disapproval. Her affectionate preference for the father in the week just preceding the present onset, followed by her tendency to turn to the mother during the illness, suggests that she was experimenting with a possessive attitude toward the father.

The presence of night terrors certainly indicates that the child was having emotional conflicts which she was unable either to express or to suppress. From her playroom activity, we know that she has an interest in and some fear of self-assertion.

She has a normal interest and curiosity in regard to the bowel and bladder functions and the generative organs. This interest in the bodily organs and their function is also extended to her surroundings; to an interest in objects about her. She likes to investigate the inside of objects and find out how they work.

The above facts suggest that the child's usual pattern—of conforming, and repressing desires for self-assertion—became unworkable because of the intensity of new aggressive and sexual drives that are normal for her age.

TREATMENT

The first step in treatment was to reassure the parents, so far as the apparent seriousness of the problem is concerned. They were helped to understand the symptom as a not-too-abnormal consequence of the child's conflict between her wishes and fears of retaliation by a parent. The advisability of allowing aggressive feelings to be expressed directly during the day was discussed. It was pointed out that the parents could help the child to work out her feelings in play. The necessity of moving both children into bedrooms of their own was stressed.

For this child, immediate therapy consisted of administering barbiturate sedation in sufficient amount to tide her through the acute phase without more episodes of sustained terror. A nursery school experience was suggested, to afford the child greater opportunity for aggressive play than her parents could provide for her.

Four months later, the mother reported that the night terrors had not recurred since the above regime was instituted. She stated that the child has been "her old self" except that she is more openly self-assertive in ways which seem entirely acceptable to the parents.

CLINICO-PATHOLOGICAL CONFERENCE

Directed by: E. Clarence Rice, M.D.
Assisted by: June Pollack, M.D.
By Invitation: Bernice Wedum, M.D.

This ten-day-old male was admitted to the Children's Hospital because of pallor and abdominal pain of one day's duration. The patient was born at term, the product of a normal spontaneous delivery, the weight at birth of seven pounds, being six and one-half ounces. The infant had a normal neonatal course and was asymptomatic until the morning of admission. At 2 a.m. on the morning he was admitted to Children's Hospital, the patient took very little nourishment and for the ensuing six hours seemed very restless. At 8 a.m. he drew up his legs and screamed for 45 minutes as if he were in pain. The attending physician diagnosed the case as "colic" and prescribed twenty drops of a pink liquid medicine. Prior to receiving this medication, the infant was noted to be very pale, and because of increasing pallor immediate hospitalization was advised. En route to the hospital, the infant became cyanotic.

The parents and one other child, aged eighteen months, were living and well.

Physical examination revealed a well-developed, well-nourished white male, who appeared acutely ill and was markedly cyanotic. The temperature was 95 degrees. The fontanelle was normal for his age and the eyes, ears, nose and throat showed no abnormalities. The respirations were very shallow with some intercostal retraction; the rate was 32 per minute. The lungs were clear to percussion. The heart rate was 160 per minute. The sounds were of good quality but a diastolic gallop rhythm was noted. No murmurs were heard. The liver extended four fingerbreadths below the right costal margin. The spleen was not palpable. The bowel sounds were absent. The femoral pulse could not be felt. Rectal examination revealed no masses and no blood was seen on the examining finger.

Blood examinations disclosed hemoglobin of 13 grams with 3.9 million red blood cells and 24,600 white blood cells; neutrophils 31 per cent, band forms 1 per cent, young forms 1 per cent, lymphocytes 63 per cent and eosinophils 4 per cent.

Roentgenogram of the chest in the anterior-posterior and lateral positions indicated the cardiac silhouette to be enlarged to the left, the contour suggesting a developmental anomaly of the heart. Examination indicated no evidence of pathology in the lungs or abdomen.

Electrocardiogram revealed a sinus tachycardia with a rate of 136 per minute, the PR interval being 0.16 seconds. The axis was normal with low

upright T_1, T_2, and T_3. RS and T in leads V_1–V_6 were within normal limits.

After the infant was placed in an oxygen tent, the cyanosis became less marked. Shortly after admission a small amount of mucus and blood was passed by rectum. Therapy included 5 per cent glucose in distilled water by slow intravenous drip and 0.1 milligram of cedilanid intravenously. The following morning the respirations were still very shallow and there was no change in size of the liver. Death occurred at 8:40 a.m., twenty-one hours after admission.

DISCUSSION

Dr. Bernice Wedum

For the points brought out in the following discussion let me first express my indebtedness to Dr. Helen B. Taussig's book, "Congenital Malformations of the Heart," and to the collection of pathological specimens at Children's Hospital, which Dr. E. Clarence Rice has built up over the past fifteen years. These have been a fruitful source of study for me and for the residents in pathology. I have also drawn from cases which I have followed on weekly rounds on the Cardiac-Surgical Service of the Johns Hopkins Hospital.

Initially, let me stress the great care with which all clinical procedures must be performed. Physical examination of the heart must include careful attention to the character of the second heart sound and the location of its point of maximal intensity, the character of the pulses in all four extremities, and blood pressure readings in both arms and legs. The distribution of the cyanosis should be noted, paying especial attention to variations in intensity between the hands and feet, noting any differences between the right and left hands.

The careful evaluation of quality, duration, intensity and pitch of murmurs which is of real importance in rheumatic heart disease is of less significance in congenital heart disease, especially in small infants. However, it is important to know whether a murmur is present or not, whether it is continuous—and it is helpful in some instances to know how well the murmur is heard in the back. The character and rate of the respirations are of the greatest importance. When palpating the liver, one should always note whether it pulsates and whether or not jugular pulsations are present.

The precordial electrocardiograms must be taken with special care in small infants since, for example, V_5 resembles V_2 if there is a continuous film of electrode jelly between the two positions. Catheterization studies are particularly difficult to do without technical errors and are not ordinarily done on children under one year of age. Angiocardiograms are more frequently done and are of distinct value in determining whether a pulmo-

nary artery is present and in some cases whether the aorta arises from the right ventricle. In a cyanotic infant, a careful physical and fluoroscopic examination with electrocardiograms usually provides enough information for an accurate diagnosis. In an acyanotic infant, the diagnosis is often much more difficult to make and one must either wait until the child is old enough for catheterization studies, or, in some cases, do an exploratory thoracotomy.

In evaluating the data obtained from the foregoing procedures, one seeks an answer to the following questions:

1. What chambers or great vessels are enlarged? Are both ventricles present and in normal position?

The procedure of greatest value is fluoroscopic or x-ray examination in the anterior-posterior and oblique positions using barium. Of almost equal value is the electrocardiogram with unipolar precordial leads. When a high-peaked P wave is present in lead II, it indicates enlargement of the right auricle although the right auricle can be enlarged without this finding being present. Fluoroscopic examination cannot be properly done unless one is thoroughly accommodated.

We have noticed recently in studying two cases of single ventricle, which have come to autopsy, that the heart was unexpectedly small in the left anterior oblique position compared to its size in the anterior-posterior position. It is a point we hope to check with further studies.

In the case under consideration, there is slight enlargement in the left anterior-oblique position. I can only say that there is slight, but probably generalized, cardiac enlargement.

2. Are the great vessels both present and in normal position? Their branches?

Careful auscultation of the second sound at the base is of real value. If it is extremely clear and pure it strongly suggests that only one set of semilunar valves is closing and that only one great vessel is present. This finding in a child with a suspected tetralogy of Fallot, in combination with either a very faint murmur or none, is evidence that pulmonary atresia is present and that the blood reaching the lungs is entering them by way of a patent ductus arteriosus. Such children must be carefully watched since closure of the ductus is often fatal under these circumstances. Increasing disability and increasing polycythemia are indications for early surgery in such children.[4]

The appearance of the shadow of the great vessels shown by roentgen examination is of great assistance in determining their position, since the shadow will be narrowed in the anterior-posterior position and broadened in the left anterior-oblique position in the usual type of transposition. An

examination of the x-rays reveals these findings in the case under discussion and I believe that the great vessels are transposed.

3. Is the blood supply to the body normal or diminished?

Palpation of the peripheral pulses is the most helpful procedure. If all four pulses are weak or almost imperceptible one may suspect that very little blood is leaving the left ventricle and that there is probably aortic atresia or stenosis. One should also think of all four pulmonary veins draining into the right auricle in connection with such a finding. In malformations compatible with a longer life—such as a large auricular septal defect or a large patent ductus arteriosus—the growth of the child is retarded because the body is deprived of the large amount of blood which recirculates through the lungs.

In this patient the femoral pulses were not palpable. This immediately suggests coarctation of the aorta but we are on shaky ground because we have here a child who is in shock with a temperature of 95° F, who may have had an intussusception. We do not know whether the radial pulses were palpable. The possibility of coarctation must be borne in mind, but we must be willing to discard it if further evidence makes this lesion seem unlikely.

4. Is the blood supply to the lungs normal, excessive or diminished?

Careful fluoroscopy is the best means of answering the question although roentgenograms will serve in most cases. One must examine the vascular markings both at the hilar and peripheral lung fields since children with tetralogy of Fallot may have rather dense central vascular markings because of polycythemia and development of collateral circulation, however, the peripheral lung fields will have a clear ground glass appearance.

The vascular markings in the lungs are normal or if anything a little increased in this patient.

5. Is the coronary circulation normal?

If there is low voltage throughout the entire electrocardiogram or if flattening of the T waves in lead I and the precordial lead is present, one may suspect that the coronary arteries are receiving mostly venous blood, which means either that the aorta arises from the right ventricle or that there is a large amount of venous blood reaching the left ventricle. Here the voltage is reduced in all leads. This, along with the roentgenographic appearance strongly suggests that the aorta is arising from the right ventricle.

6. Are the systemic and pulmonic venous returns normal?

When all the pulmonary veins drain into the right auricle the vascular markings of the lungs are so greatly increased that one can suspect these malformations simply from the appearance of the roentgenograms. In my experience there is one other malformation which, in the majority of cases,

is accompanied by an anomalous venous return, and that is levocardia with situs inversus. In all other cases either catheterization or angiocardiographic studies are necessary to determine whether an anomaly of the venous return is present.

7. Is an arteriovenous shunt present?

Study of the lung fields will reveal whether or not there is recirculation due to a shunt. The retardation of growth in older children, which results from the decreased amount of blood going to the other parts of the body is a helpful clue. In this child I do not believe we can say for certain whether such a condition is present after studying the lung fields.

8. Is a venous arterial shunt present?

The presence of cyanosis of equal distribution in the lips, fingers, and toes, which increases on crying, is almost pathognomonic of a venous arterial shunt. If the cyanosis is more intense in the feet than in the hands, it suggests coarctation of the aorta proximal to the ductus arteriosus, with a large amount of venous blood going directly through the ductus arteriosus to the descending aorta. If the right hand is not cyanotic, there is clearly a patent ductus arteriosus through which blood is flowing from the pulmonary artery in a reversed direction due to pulmonary hypertension.

If the cyanosis is more intense in the hands than in the feet, as in this case, it suggests a coarctation with transposition of the great vessels, with less cyanotic blood flowing from the left ventricle into the transposed pulmonary artery through the ductus arteriosus to the feet. It should be remembered that any child with failure due to any form of heart disease may develop mild peripheral cyanosis due to decreased cardiac output. It also never should be forgotten that a baby with a malformation ordinarily causing cyanosis, need not have visible cyanosis if anemia is present.

9. Is cerebral anoxemia present?

The character of the respirations is the finding which answers the question. Ordinarily when a child is in congestive failure, the respirations are markedly increased; indeed, increase in the respiratory rate is the earliest sign of congestive failure in infants. If the respirations are decreased, as they are in this child, it is a clear indication that cerebral anoxemia is present, which suggests that the brain is receiving largely venous blood. This again suggests that the aorta is arising from the right ventricle. These children, when they have lesions compatible with a longer life, also have characteristic "spells" which can be relieved by morphine and by placing the patient in the knee-chest position.

In this case the respiratory rate was 32 and there was clearly a marked degree of cerebral anoxemia.

10. Is congestive failure present?

Increase in the respiratory rate is the first sign of congestive failure. This is later followed by enlargement of the liver and peripheral edema. When congestive failure is characterized by an abrupt onset as in this patient, one always suspects that a ductus arteriosus has closed or has become considerably narrowed, rendering a malformation which previously was compatible with life, incompatible with same.

In summary, this is essentially the story of an infant who was well for a few days following birth, but who suddenly developed cyanosis and congestive failure and died in twenty-four hours. One is impressed with the rapidity with which the congestive heart failure developed, the marked enlargement of the liver suggesting that there was a great strain on the right ventricle. It is this, more than the absence of femoral pulses and cyanosis of the hands, that suggests the diagnosis of preductal coarctation in this case. The appearance of the shadows of the great vessels, the low voltage of the electrocardiogram and the presence of cerebral anoxemia strongly suggest that the aorta arises from the right ventricle. I would list my diagnoses in the following order:

1. Transposition of the great vessels with preductal (infantile) coarctation and a ductus arteriosus which has recently closed or is almost closed.
2. Transposition of the great vessels with closed septa and a patent ductus arteriosus which has recently closed.
3. Extreme dextroposition of the aorta (extreme tetralogy of Fallot) with pulmonary atresia and a ductus arteriosus which has recently closed or almost closed.

PATHOLOGIC DISCUSSION

Dr. Pollack:

At autopsy, the body was that of a fairly well developed, well nourished white male infant weighing 3459 grams. There was slight generalized cyanosis. Grossly the only organ which revealed any abnormality was the heart.

The usual contour of the heart was altered; a small bulging segment was seen in the left upper corner. The systemic venous return was normal. The right auricle was dilated and the foramen ovale was patent. The tricuspid valve was normal in position, directing the flow of blood to a single ventricle, which communicated with a rudimentary outlet chamber in its left upper portion, forming the bulbous segment of the ventricle. From this outlet chamber, the aorta arose anteriorly and to the left of the pulmonary artery. This rudimentary cavity was partially separated from the main compartment by a prominent muscular ledge; the communication measured

0.7 x 0.4 cm. The single ventricle led to the pulmonary artery which was guarded by a normal pulmonary valve which was located to the right and posterior to the origin of the aorta. The pulmonary artery bifurcated normally and the ductus arteriosus was patent.

The aorta arose from the rudimentary outlet chamber and was guarded by a normal aortic valve. The arch of the aorta narrowed to a constricted opening of less than 0.5 mm in diameter which was located proximal to the junction of the ductus arteriosus.

The four pulmonary veins emptied into the left auricle which was smaller than the right one. Its communication with the single ventricle was guided by a well formed bicuspid valve, the latter cusp of which was inserted into the lateral wall of the rudimentary chamber thus favoring the passage of the oxygenated blood from the left auricle to the outlet chamber.

Microscopically the myocardial fibers were seen to contain numerous irregular, patchy cytoplasmic vacuolizations.

The alveolar pattern of the lungs was altered, the pulmonary septa were thickened and some alveoli were filled with sheets of desquamating epithelial cells, strands of fibrin or cellular debris and a few red blood cells. The bronchioles contained the same material as that seen in the alveoli. Many of the pulmonary arterioles showed medial or adventitial thickening.

The only other abnormality noted was some fatty vacuolization of the hepatic cells.

The final diagnoses were as follows:

1. Developmental anomalies of the heart:
   a. Single ventricle with a rudimentary outlet chamber from which arises the aorta.
   b. Preductal coarctation of the aorta.
   c. Transposition of the great vessels.
   d. Patent foramen ovale.
   e. Patent ductus arteriosus.
2. Myocardial degeneration.
3. Aspiration pneumonitis.
4. Fatty metamorphosis of the liver.

ANNUAL OUTING

The Editorial Board of *Clinical Proceedings* expresses its appreciation to members of the attending staff whose contributions made possible the annual outing on Memorial Day, May 30, in the Meadowbrook area of Rock Creek Park, Silver Spring, Md. Special thanks are due to Mr. Earl F. C. Payne, Regional Manager for Mead Johnson and Company, who provided the soft drinks.

Dr. David A. St. Martin, Chief Resident Physician, and Dr. Stanley I. Wolf were co-chairmen of the event for the resident staff and Dr. John A. Washington was coach for the softball team of the attending staff. The title of "Softball Queen," which is awarded annually on the basis of popular vote, was won this year by Miss Hope Isherwood, assistant administrator of The Children's Hospital. Assistance in getting food to the picnic area and in setting up the refreshment facilities was given by Mr. Jacob Smith and Mr. Dorthan Williams.

Seventy-five persons saw the residents hold the lead in a hard-fought contest (13–9) before the participants got rained out. The residents had, however, made good their threat to avenge defeat the two previous years at the hands of the attending staff.

Proceeds of the affair will be used to defray some of the expenses of publishing *Clinical Proceedings*.